NMCP COVID-19 Literature Report #32: Friday, 24 July 2020

Update: Starting with this report, we are shifting to a weekly publication. The website will be updated throughout the week with items of interest, and on Fridays a report summarizing the week will be generated and formalized into a document for distribution.

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Purpose: These reports are curated collections of current research, evidence reviews, and news regarding the COVID-19 pandemic; they are biweekly, planned for Tuesdays and Fridays. Please feel free to reach out with questions and suggestions for future topics.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL, along with the case-sensitive password "NMCPfinest".

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, things are changing rapidly, with new research and potentially conflicting literature published daily.

Statistics

Global

15,559,865 confirmed cases and 634,405 deaths in 188 countries/regions

United States*

top 5 states by cases (Virginia is ranked 15th)

	TOTAL US	CA	NY	FL	TX	NJ
Confirmed Cases	15,559,865	430,773	409,697	402,312	373,037	177,887
Tested	48,794,970	6,778,304	5,368,338	3,210,942	3,164,656	1,859,638
Recovered	NA	NA	72,466	NA	203,826	31,925
Deaths	144,469	8,201	32,594	5,653	4,622	15,730

^{*}see <u>census.gov</u> for current US Population data; NA: not all data available

<u>JHU CSSE</u> as of 1100 EDT 24 July 2020

Virginia	Total	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	82,364	1,953	822	1,356	2,582	1,165	865	3,119
Hospitalized	7,515	180	48	69	155	107	83	177
Deaths	2,067	24	4	14	20	21	45	41

VA DOH as of 1100 EDT 24 July 2020

Selected Primary Literature

Recently published in peer-reviewed journals

<u>Thorax</u>: Face coverings and mask to minimise droplet dispersion and aerosolisation: a video case study (24 July 2020)

"To evaluate the effectiveness of the Centers for Disease Control and Prevention (CDC) recommended one- and two-layer cloth face covering against a three-ply surgical mask, we challenged the cloth covering against speaking, coughing and sneezing. The one-layer covering was made using 'quick cut T-shirt face covering (no-sew method)' and the twolayer covering was prepared using the sew method prescribed by CDC.1 To provide visual evidence of the efficacy of face coverings we used a tailored LED lighting system (GS Vitec MultiLED PT) along with a high-speed camera (nac MEMRECAM HX-7s) to capture the light scattered by droplets and aerosols expelled during speaking, coughing and sneezing while wearing different types of masks (figure 1 and online supplementary video). The video for speaking was captured at 850 frames/s (fps) and for coughing and sneezing a frame rate of 1000 fps was used due to the higher expulsion speeds. Frames of the captured videos were pre-processed by applying a calibration and a two-axis stabilisation. 2 We used a healthy volunteer without any respiratory infection and informed consent was obtained before conducting the experiments. The cough performed was voluntary and to induce a sneeze the subject used a tissue paper to stimulate the mucus membrane of the nasal cavity. The cloth coverings were made from 175 GSM cotton fabric with a thread count of 170 TPI and the surgical mask used was a three-ply Bao Thach face mask."

JAMA Otolaryngol Head Neck Surg: SARS-CoV-2 Virus Isolated From the Mastoid and Middle Ear: Implications for COVID-19 Precautions During Ear Surgery (23 July 2020)

"We present confirmation of SARS-CoV-2 colonization of the middle ear and mastoid in 2 of 3 patients....

This study confirms the presence of SARS-CoV-2 virus in the middle ear and mastoid, with significant implications for otolaryngology procedures. Similar to procedures of the nose, mouth, and airway, droplet precautions during ear surgery are warranted for patients with COVID-19 owing to risk of infection to health care personnel.1 Droplet precautions (including eye protection and proper N95 level mask) are warranted for outpatient procedures involving the middle ear due to proximity to these potentially infectious spaces. Given the high asymptomatic rate of COVID-19 cases, caution is warranted for all elective ear surgery, and negative status by testing is indicated."

<u>NEJM</u>: Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19 (23 July 2020)

"We conducted a multicenter, randomized, open-label, three-group, controlled trial involving hospitalized patients with suspected or confirmed Covid-19 who were receiving

either no supplemental oxygen or a maximum of 4 liters per minute of supplemental oxygen....

A total of 667 patients underwent randomization; 504 patients had confirmed Covid-19 and were included in the modified intention-to-treat analysis. As compared with standard care, the proportional odds of having a higher score on the seven-point ordinal scale at 15 days was not affected by either hydroxychloroquine alone (odds ratio, 1.21; 95% confidence interval [CI], 0.69 to 2.11; P=1.00) or hydroxychloroquine plus azithromycin (odds ratio, 0.99; 95% CI, 0.57 to 1.73; P=1.00). Prolongation of the corrected QT interval and elevation of liver-enzyme levels were more frequent in patients receiving hydroxychloroquine, alone or with azithromycin, than in those who were not receiving either agent.

Among patients hospitalized with mild-to-moderate Covid-19, the use of hydroxychloroquine, alone or with azithromycin, did not improve clinical status at 15 days as compared with standard care."

<u>Clin Microbiol Infect</u>: Viable SARS-CoV-2 in various specimens from COVID-19 patients (22 July 2020)

"To demonstrate whether various clinical specimens contain the viable virus, we collected naso/oropharyngeal swabs, saliva, urine, and stool from five COVID-19 patients and performed a quantitative polymerase chain reaction (qPCR) to assess viral load. Specimens positive by qPCR were subjected to virus isolation in Vero cells. We also used urine and stool samples to intranasally inoculate ferrets and evaluated the virus titers in nasal washes on 2, 4, 6, and 8 days post-infection (dpi).

SARS-CoV-2 RNAs were detected in all naso/oropharyngeal swabs, saliva, urine, and stool samples collected between days 8 to 30 of the clinical course. Notably, viral loads in urine, saliva, and stool samples were almost equal to or higher than those in naso/oropharyngeal swabs (urine 1.08±0.16 – 2.09±0.85 log10 copies/ml, saliva 1.07±0.34 – 1.65±0.46 log10 copies/ml, stool 1.17±0.32 log10 copies/ml, naso/oropharyngeal swabs 1.18±0.12 – 1.34±0.30 log10 copies/ml). Further, viable SARS-CoV-2 was isolated from naso/oropharyngeal swabs and saliva of COVID-19 patients, as well as nasal washes of ferrets inoculated with patient urine or stool.

Viable SARS-CoV-2 was demonstrated in saliva, urine, and stool from COVID-19 patients up until days 11 to 15 of the clinical course. This result suggests that viable SARS-CoV-2 can be secreted in various clinical samples as well as respiratory specimens."

<u>JAMA Netw Open</u>: Association of Interleukin 7 Immunotherapy With Lymphocyte Counts Among Patients With Severe Coronavirus Disease 2019 (COVID-19) (22 July 2020)

"The findings of this study suggest that IL-7 can be safely administered to critically ill patients with COVID-19 without exacerbating inflammation or pulmonary injury. IL-7 was associated with lymphocytes returning to a reference level, appearing to reverse a

pathologic hallmark of COVID-19. Importantly, previous studies have reported that IL-7— associated restoration of lymphocyte numbers enhanced the activity of antiviral agents.6 A limitation of the current study is that no phenotypic or functional studies of immune cells were conducted. Administration of IL-7 alone or in combination with other therapies warrants serious consideration for patients with COVID-19 and evidence of immunosuppression."

<u>JAMA Netw Open</u>: Comparison of Unsupervised Home Self-collected Midnasal Swabs With Clinician-Collected Nasopharyngeal Swabs for Detection of SARS-CoV-2 Infection (22 July 2020)

"Study participants were recruited from symptomatic outpatients testing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—positive and symptomatic health care workers presenting to drive-through clinics. Participants were provided test kits for unsupervised home self-collection of a midnasal swab. Home swab performance was compared with clinician-collected nasopharyngeal swabs, which were collected by medical assistants and nurses....

Unsupervised home midnasal swab collection was comparable to clinician-collected nasopharyngeal swab collection for detection of SARS-CoV-2 in symptomatic patients, particularly those with higher viral loads. During this rapidly evolving pandemic, we enrolled 185 individuals presenting for SARS-CoV-2 testing, including 41 with positive test results. We used novel home-based swab self-collection and rapid delivery services, thus avoiding participant contact with the health care system."

<u>Nature</u>: Potent neutralizing antibodies directed to multiple epitopes on SARS-CoV-2 spike (22 July 2020; previously posted to <u>bioRxiv</u> 16 Jun 2020)

"The SARS-CoV-2 pandemic rages on with devasting consequences on human lives and the global economy1,2. The discovery and development of virus-neutralizing monoclonal antibodies could be one approach to treat or prevent infection by this novel coronavirus. Here we report the isolation of 61 SARS-CoV-2-neutralizing monoclonal antibodies from 5 infected patients hospitalized with severe disease. Among these are 19 antibodies that potently neutralized the authentic SARS-CoV-2 in vitro, 9 of which exhibited exquisite potency, with 50% virus-inhibitory concentrations of 0.7 to 9 ng/mL. Epitope mapping showed this collection of 19 antibodies to be about equally divided between those directed to the receptor-binding domain (RBD) and those to the N-terminal domain (NTD), indicating that both of these regions at the top of the viral spike are immunogenic. In addition, two other powerful neutralizing antibodies recognized quaternary epitopes that overlap with the domains at the top of the spike. Cryo-electron microscopy reconstructions of one antibody targeting RBD, a second targeting NTD, and a third bridging two separate RBDs revealed recognition of the closed, "all RBD-down" conformation of the spike. Several of these monoclonal antibodies are promising candidates for clinical development as potential therapeutic and/or prophylactic agents against SARS-CoV-2."

<u>NEJM</u>: Rapid Scaling Up of Covid-19 Diagnostic Testing in the United States — The NIH RADx Initiative (22 July 2020)

"Expanding the capacity, throughput, speed of returning results, analytic performance, and regional placement of diagnostic technologies is urgently needed and, if successful, will contribute importantly to the current national efforts to curb the Covid-19 pandemic and help to reduce inequities for underserved populations. As we embark on this initiative, the challenges ahead are considerable, and the timetable is truly daunting. Aiming to achieve this rapid evaluation, validation, and scale-up has rarely, if ever, been attempted at this pace. However, the NIH is in a position to serve as a "venture investment" organization and is currently striving to operate in that entrepreneurial spirit. The success of the RADx program will depend on truly innovative ideas coming forward from the minds and laboratories of technology developers, a robust and rapidly responsive expert evaluation system, extensive collaborations in validation and scale-up with experts from all sectors, and strong community partnerships to support testing availability and uptake. All these partners are profoundly energized by a sense of urgency, opportunity, and responsibility to provide testing at scale in the face of this global pandemic."

<u>Ann Intern Med</u>: Feasibility of Separate Rooms for Home Isolation and Quarantine for COVID-19 in the United States (21 July 2020)

"More than 1 in 5 U.S. homes, housing about one quarter of all Americans, lack sufficient space and plumbing facilities to comply with recommendations to isolate or quarantine to limit household spread of COVID-19. This proportion is particularly high among homes occupied by minority and poor individuals and among apartments, a pattern that mirrors both the high incidence of COVID-19 in those groups and racial discrimination in access to housing that was federal policy until the 1960s and, unfortunately, persists today."

<u>JAMA Intern Med</u>: Seroprevalence of Antibodies to SARS-CoV-2 in 10 Sites in the United States, March 23-May 12, 2020 (21 July 2020)

"Question: What proportion of persons in 10 US sites had detectable antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from March 23 to May 12, 2020?

Findings: In this cross-sectional study of 16 025 residual clinical specimens, estimates of the proportion of persons with detectable SARS-CoV-2 antibodies ranged from 1.0% in the San Francisco Bay area (collected April 23-27) to 6.9% of persons in New York City (collected March 23-April 1). Six to 24 times more infections were estimated per site with seroprevalence than with coronavirus disease 2019 (COVID-19) case report data.

Meaning: For most sites, it is likely that greater than 10 times more SARS-CoV-2 infections occurred than the number of reported COVID-19 cases; most persons in each site, however, likely had no detectable SARS-CoV-2 antibodies."

NEJM: Rapid Decay of Anti-SARS-CoV-2 Antibodies in Persons with Mild Covid-19 (21 July 2020)

"We evaluated persons who had recovered from Covid-19 and referred themselves to our institution for observational research....

A total of 31 of the 34 participants had two serial measurements of IgG levels, and the remaining 3 participants had three serial measurements. The first measurement was obtained at a mean of 37 days after the onset of symptoms (range, 18 to 65), and the last measurement was obtained at a mean of 86 days after the onset of symptoms (range, 44 to 119)....

Our findings raise concern that humoral immunity against SARS-CoV-2 may not be long lasting in persons with mild illness, who compose the majority of persons with Covid-19. It is difficult to extrapolate beyond our observation period of approximately 90 days because it is likely that the decay will decelerate."

<u>Pediatrics</u>: COVID-19 Disease Severity Risk Factors for Pediatric Patients in Italy (20 July 2020)

"To describe the epidemiological and clinical characteristics of Coronavirus disease2019 (COVID-19) pediatric cases aged below 18 years in Italy.

Data from the national case-based surveillance system of confirmed COVID-19 infections until May 8, 2020, were analyzed. Demographic and clinical characteristics of subjects were summarized by age groups (0-1, 2-6, 7-12, 13-18 years), and risk factors for disease severity were evaluated using a multilevel (clustered by region) multivariable logistic regression model. Furthermore, a comparison among children, adults and elderly was performed.

Pediatric cases (3,836) accounted for 1.8% of total infections (216,305), the median age was 11 years, 51.4% were males, 13.3% were hospitalized, and 5.4% presented underlying medical conditions. The disease was mild in 32.4% of cases and severe in 4.3%, particularly in children ≤6 years old (10.8%); among 511 hospitalized patients, 3.5% were admitted in Intensive Care Unit (ICU), and four deaths occurred. Lower risk of disease severity was associated with increasing age and calendar time, whereas a higher risk was associated with pre-existing underlying medical conditions (OR=2.80, 95% CI 1.74-4.48). Hospitalization rate, admission in ICU, disease severity, and days from symptoms onset to recovery significantly increased with age among children, adults and elderly."

Preprints—not yet peer-reviewed papers

<u>arXiv</u>, <u>bioRxiv</u>, and <u>medRxiv</u> are preprint servers: "[T]hese are preliminary reports that have not been peer-reviewed. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information."

medRxiv: The Infectious Nature of Patient-Generated SARS-CoV-2 Aerosol (posted 21 July 2020)

"Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission causing coronavirus disease 2019 (COVID-19) may occur through multiple routes. We collected aerosol samples around six patients admitted into mixed acuity wards in April of 2020 to identify the risk of airborne SARS-CoV-2. Measurements were made to characterize the size distribution of aerosol particles, and size-fractionated, aerosol samples were collected to assess the presence of infectious virus in particles sizes of >4.1 μm, 1-4 μm, and <1 μm in the patient environment. Samples were analyzed by real-time reverse-transcriptase polymerase chain reaction (rRT-PCR), cell culture, western blot, and transmission electron microscopy (TEM). SARS-CoV-2 RNA was detected in all six rooms in all particle size fractions (>4.1 μm, 1-4 μm, and <1 μm). Increases in viral RNA during cell culture of the virus from recovered aerosol samples demonstrated the presence of infectious, replicating virions in three <1 µm aerosol samples (P<0.05). Viral replication of aerosol was also observed in the 1-4 µm stage but did not reach statistical significance (0.05<P<0.10). Western blot and TEM analysis of these samples also showed evidence of viral proteins and intact virions. The infectious nature of aerosol collected in this study further suggests that airborne transmission of COVID-19 is possible, and that aerosol prevention measures are necessary to effectively stem the spread of SARS-CoV-2."

<u>medRxiv</u>: Concurrent human antibody and TH1 type T-cell responses elicited by a COVID-19 RNA vaccine (posted 20 July 2020)

"An effective vaccine is needed to halt the spread of the SARS-CoV-2 pandemic. Recently, we reported safety, tolerability and antibody response data from an ongoing placebocontrolled, observer-blinded phase 1/2 COVID-19 vaccine trial with BNT162b1, a lipid nanoparticle (LNP) formulated nucleoside-modified messenger RNA encoding the receptor binding domain (RBD) of the SARS-CoV-2 spike protein. Here we present antibody and T cell responses after BNT162b1 vaccination from a second, non-randomized open-label phase 1/2 trial in healthy adults, 18-55 years of age. Two doses of 1 to 50 µg of BNT162b1 elicited robust CD4+ and CD8+ T cell responses and strong antibody responses, with RBD-binding IgG concentrations clearly above those in a COVID-19 convalescent human serum panel (HCS). Day 43 SARS-CoV-2 serum neutralising geometric mean titers were 0.7-fold (1 µg) to 3.5-fold (50 µg) those of HCS. Immune sera broadly neutralised pseudoviruses with diverse SARS-CoV-2 spike variants. Most participants had TH1 skewed T cell immune responses with RBD-specific CD8+ and CD4+ T cell expansion. Interferon (IFN)γ was produced by a high fraction of RBD-specific CD8+ and CD4+ T cells. The robust RBD-specific antibody, T-cell and favourable cytokine responses induced by the BNT162b1 mRNA vaccine suggest multiple beneficial mechanisms with potential to protect against COVID-19."

<u>medRxiv</u>: Viral load of SARS-CoV-2 across patients and compared to other respiratory viruses (posted 16 July 2020)

"RT-PCR to detect SARS-CoV-2 RNA in clinical specimens was key to manage the COVID-19 pandemic. We monitored SARS-CoV-2 viral loads over time and across different patient populations. We analyzed RT-PCR results according to samples types, gender, age, and health units and compared SARS-CoV-2 viral load to other respiratory viruses, representing a total of 28,373 RT-PCR results including 22,323 SARS-CoV-2 RT-PCR. The importance of viral load to predict contagiousness and clinical prognosis is discussed."

Upcoming Events (Webinars, Calls, etc.)

WHAT: CDC Clinician Outreach and Communication Activity (COCA) Call

TOPIC: Coronavirus Disease 2019 (COVID-19) and Diabetes: The Importance of

Prevention, Management, and Support

"During this COCA Call, presenters will focus on current information about the impact and increased risk for COVID-19 complications in people with diabetes and the importance of diabetes prevention, management, and support."

WHEN: Tuesday, 28 July 2020 1400-1500 ET

DETAILS: https://emergency.cdc.gov/coca/calls/2020/callinfo 072820.asp

News in Brief

The US has passed 4 million cases of COVID-19 (JHU CSSE).

Florida – currently ranked second in cases by state – has set another coronavirus record with 173 deaths reported in one day (NPR).

Dr. Deborah Birx, referring to rising cases of coronavirus in Florida, Texas, and California: "What we have right now are essentially three New Yorks with these three major states" (Today).

Reports of reinfection with COVID-19 may be drawn-out cases, according to experts (NYT).

Testing and Research

"Future COVID-19 tests will also be able to test for influenza A and B, according to Trump administration 'testing czar' Adm. Brett Giroir, MD" (Medpage).

A French hospital is using a breathalyzer machine to detect COVID-19 (Reuters).

Officials at Yosemite national park suspect that hundreds of visitors this summer may have had coronavirus – because they tested sewage and found traces of SARS-CoV-2 (<u>Guardian</u>).

"Chile wants Covid-19 sniffer dogs to help reopen public spaces" (CNN).

Vaccine Race

The US government has contracted with Pfizer and BioNTech in a nearly \$2 billion contract for 600 million doses of a vaccine, with the first 100 million promised before the end of the year (NYT).

This pricing places COVID-19 vaccine price around the cost of a flu shot (Reuters).

As coronavirus vaccines are fast-tracked, there's still uncertainty which ones will work (Nature).

Experts say that without a vaccine, we may never get herd immunity with this virus (NPR).

Several COVID-19 vaccines under development may require more than one dose to be effective (Medpage).

Thanks, Coronavirus

The pandemic is accelerating hunger and starvation around the world (<u>PBS</u>; for a summary on food (in)security, see <u>NMCP COVID-19</u> literature report #09).

"Earthquake sensors record unprecedented drop in human activity due to pandemic. Such a sweeping effect has never been seen in the history of earthquake science" (<u>WaPo</u>; see <u>Science</u> for full text).

According to Unilever, ice cream sales were up 26% and demand for hygiene products like shampoo and deodorant were down between April and June (BBC).

Other Infectious Diseases

Trench fever – "a rare condition transmitted by body lice that plagued soldiers during World War I" – has been confirmed in 3 people in Denver (KHN).

There are 62 cases, 27 deaths, and 19 recovered patients in the latest Ebola outbreak (WHO).

Long Reads and Explainers

"Covid-19 antibody testing, long-term immunity, vaccines, herd immunity (and more!), explained" (Vox).

"How to fix the Covid-19 dumpster fire in the US" (STAT).

References

Statistics

JHU CSSE: Johns Hopkins Center for Systems Science and Engineering. Coronavirus COVID-19 Global Cases. Link: https://coronavirus.jhu.edu/map.html

VA DOH: Virginia Department of Health. COVID-19 in Virginia. Link: http://www.vdh.virginia.gov/coronavirus/

Selected Primary Literature

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Clin Microbiol Infect: Jeong HW, Kim SM, Kim HS, et al. Viable SARS-CoV-2 in various specimens from COVID-19 patients. Clin Microbiol Infect Published: July 22, 2020 DOI: https://doi.org/10.1016/j.cmi.2020.07.020 Link:

https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30427-4/fulltext

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JAMA Netw Open: McCulloch DJ, Kim AE, Wilcox NC, Logue JK, Greninger AL, Englund JA, Chu HY. Comparison of Unsupervised Home Self-collected Midnasal Swabs With Clinician-Collected Nasopharyngeal Swabs for Detection of SARS-CoV-2 Infection. JAMA Netw Open. 2020 Jul 1;3(7):e2016382. doi: 10.1001/jamanetworkopen.2020.16382. PMID: 32697321. Link: https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2768535

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News in Brief

BBC: BBC News. Unilever: Ice cream in, personal hygiene out in lockdown (23 July 2020) Link: https://www.bbc.com/news/business-53511028

CNN: CNN Health. Tatiana Arias and Christopher Ulloa. Chile wants Covid-19 sniffer dogs to help reopen public spaces (22 July 2020). Link: https://www.cnn.com/2020/07/22/health/dogs-coronavirus-sniff-public-spaces-intl/index.html

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